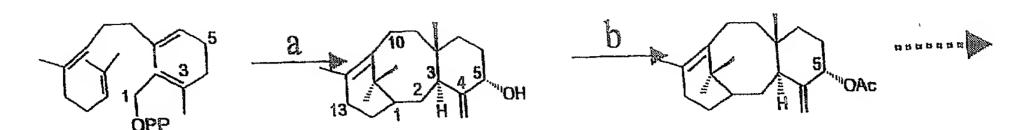
Donald L. Stephens, Jr.
Our Ref. No. 4630-59094/DLS/JOC
Inventors: Croteau et al.
For: TRANSACYLASES OF THE PACLITAXEL
BIOSYNTHETIC PATHWAY
Application No. 09/866,570, filed May 25, 2001
Mailed: September 20, 2001
Page 1 of 33

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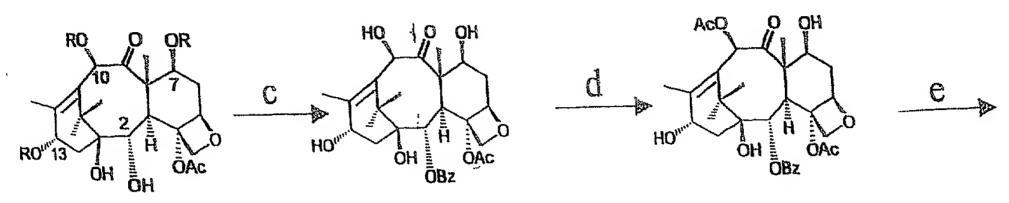




geranylgeranyl diphosphate

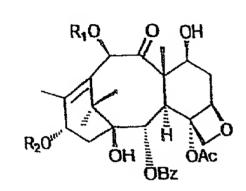
 $taxa-4(20), 11(12)-dien-5\alpha-o1$ 

taxa-4(20), 11(12)-dien-5α-yl acetate



intermediate 2-debenzoyltaxane R = H and/or Acyl 10-deacetylbaccatin III

baccatin III



Taxol:  $R_1 = Ac$  $R_2 = N-Bz$  phenylisoserinyl Donald L. Stephens, Jr.
Our Ref. No. 4630-59094/DLS/JOC
Inventors: Croteau et al.
For: TRANSACYLASES OF THE PACLITAXEL
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Tryptic Peptide Fragment Peptide Sequence

	TTLQLSSIDNLPGVR
SEQ ID NO: 29	
SEQ ID NO: 30	ILVYYPPFAGR
SEQ ID NO: 31	FTCGGFVVGVSF
SEQ ID NO: 32	KGLAEIARGEVK
	NLPNDTNPSSGYYGN
SEQ ID NO: 33	MULTADITATOSOTAGE

FIG. 2

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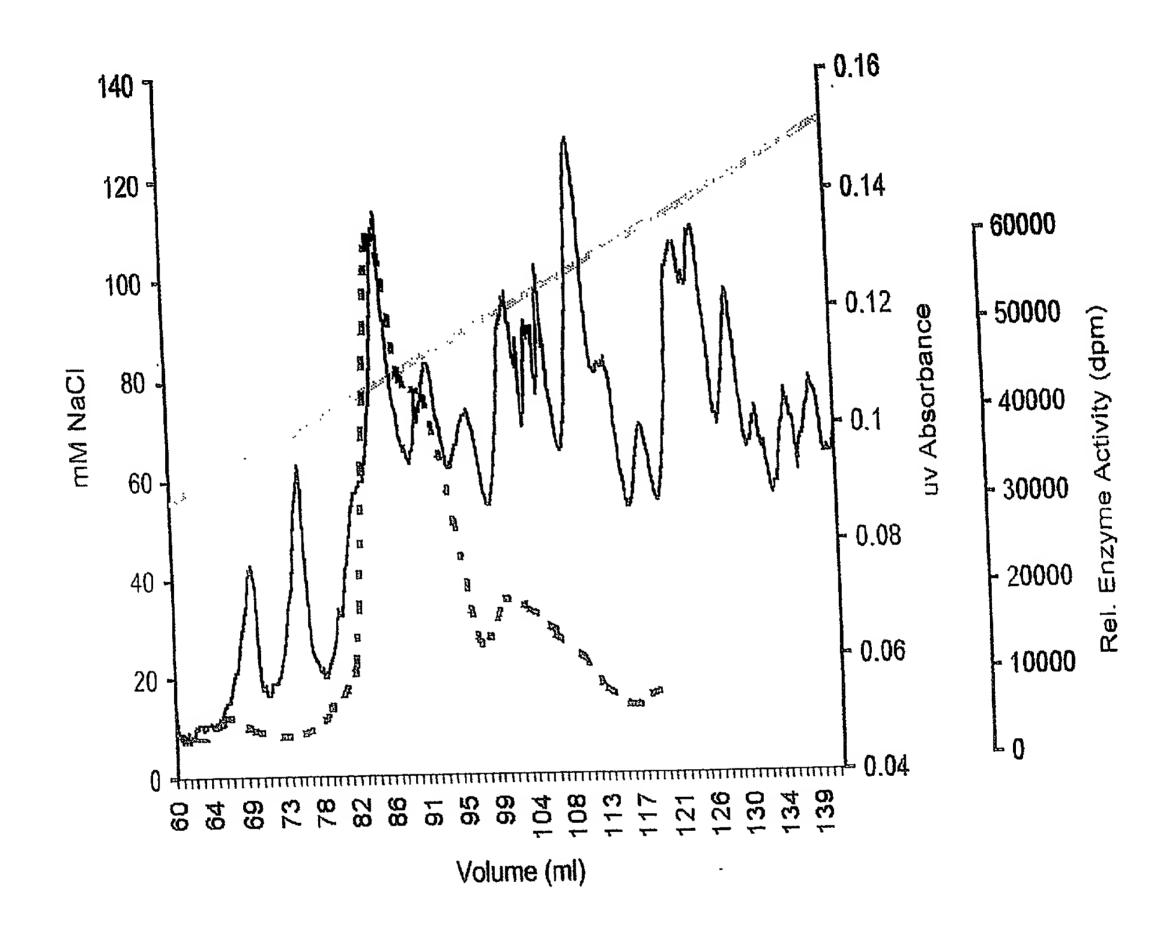


FIG. 3A



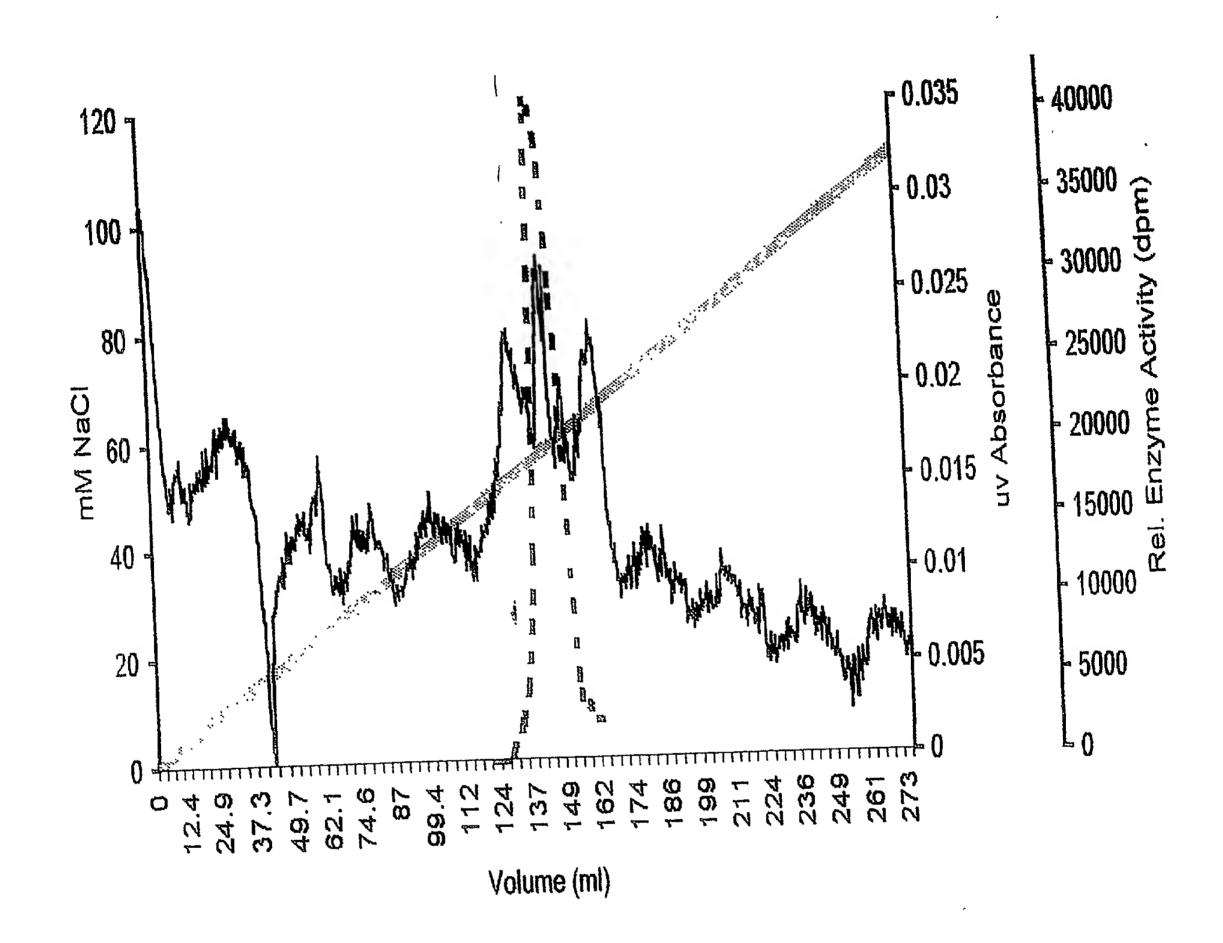


FIG. 3B

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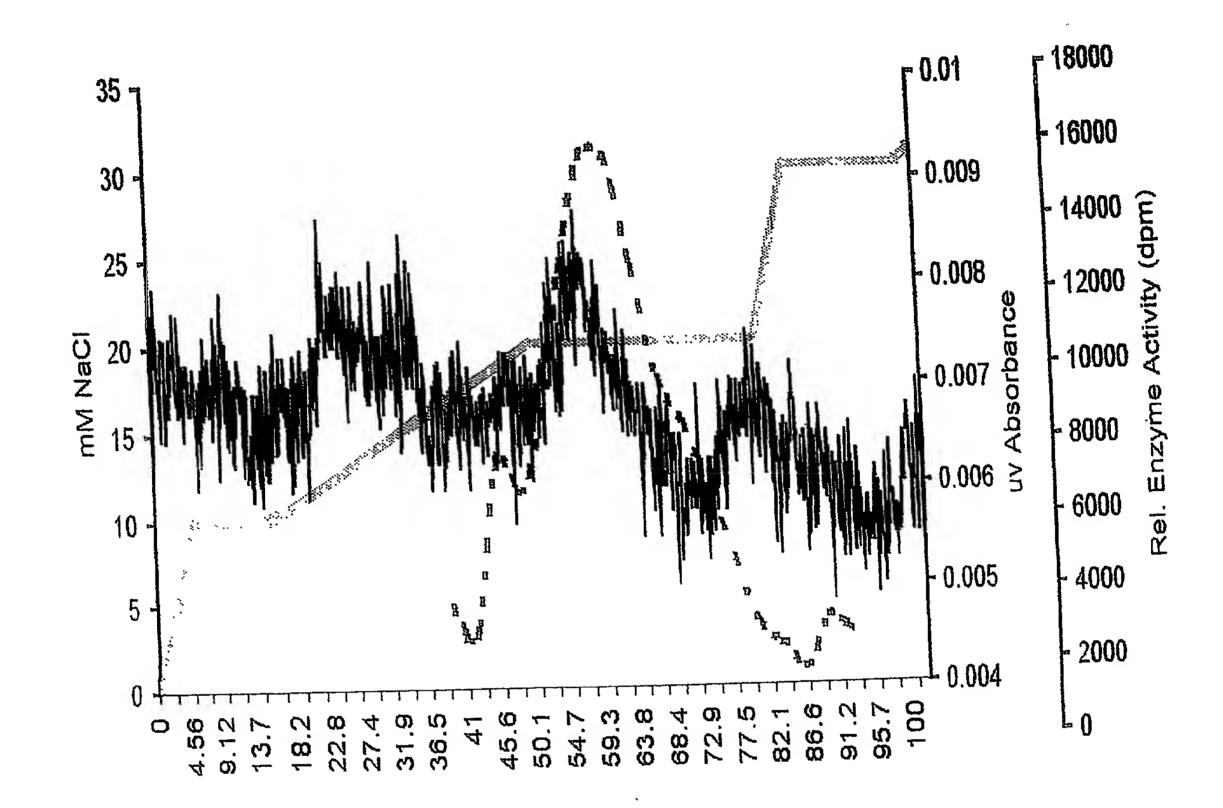


FIG. 3C

Hard Hard Hard Hard Loop of the Loop of th

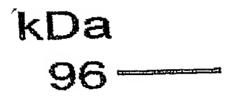




FIG. 3D

ARCHITECTURE OF

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FROM PEPTIDE FRAGMENT SEQUENCE 2

						~~=	~~	21	አሞ_ፔለ℧ኃ
NH2-	Y	Y	P	P	F	A	G	-COOH	
5′	ITA	CTI T	GTI C A	TAT	TAT	CCI A	CC	3′	AT-FOR1 (SEQ ID NO: 34)
NH2-	I	L	V	Y	Y	P	P	-COOH	7 E 2707.1

AT-FOR2 GCI 3′ 5' CCI TTT GG TAT CCI TAT (SEQ ID NO: 35) C C C C  $\mathsf{C}$  $\mathsf{C}$ A A A

FROM SEQUENCE HOMOLOGY CONSIDERATIONS

NH2-	F	Y	P	F	A	G	R	-COOH	
5′	TTC	TAT	CCI	TTC	GCI	GGI	AG	3′	AT-FOR3
	T	C		T	C	С			(SEQ ID NO: 36)
					A	A			

FIG. 4

 $(a,b) = \mathbf{a} \cdot (\mathbf{a} \cdot \mathbf{b}) = (a,b) \cdot (a,b) = (a,b) \cdot (a,b)$ 



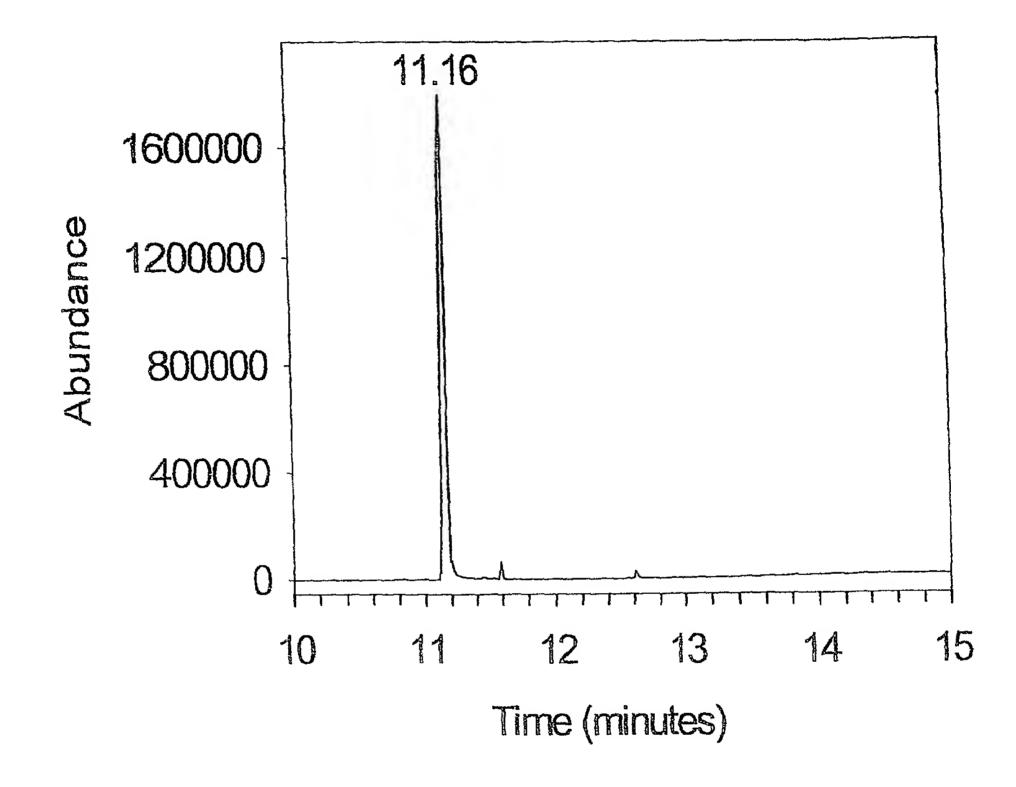


FIG. 5A

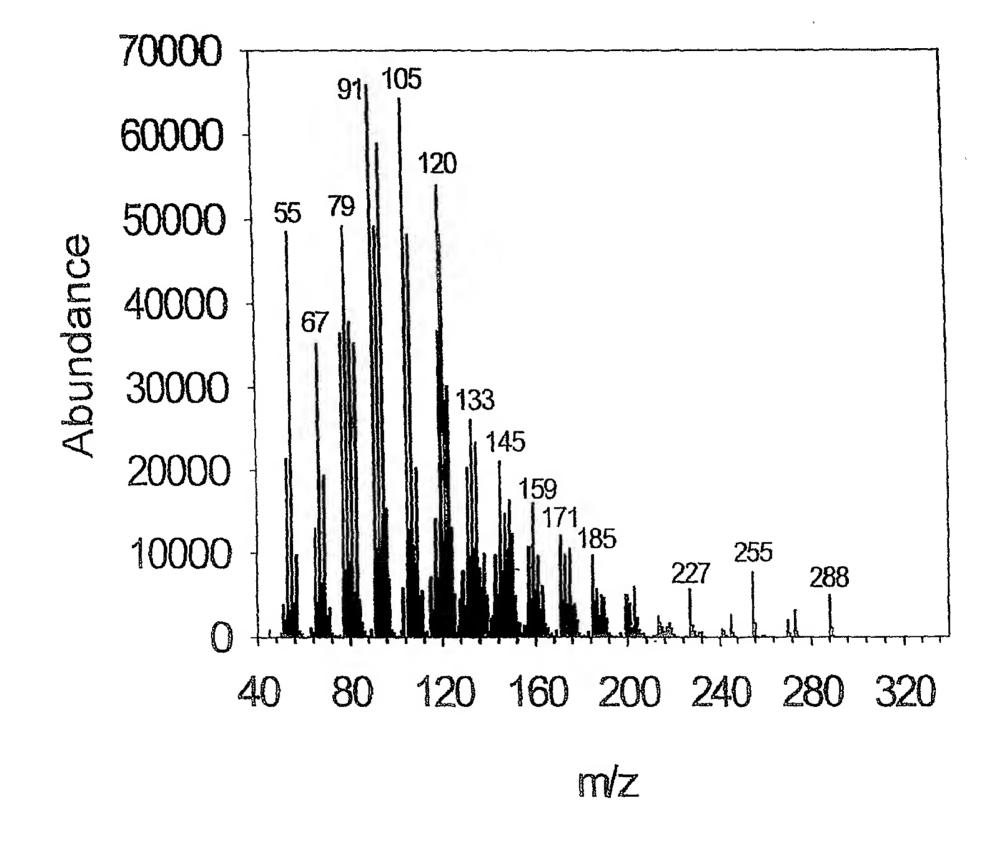
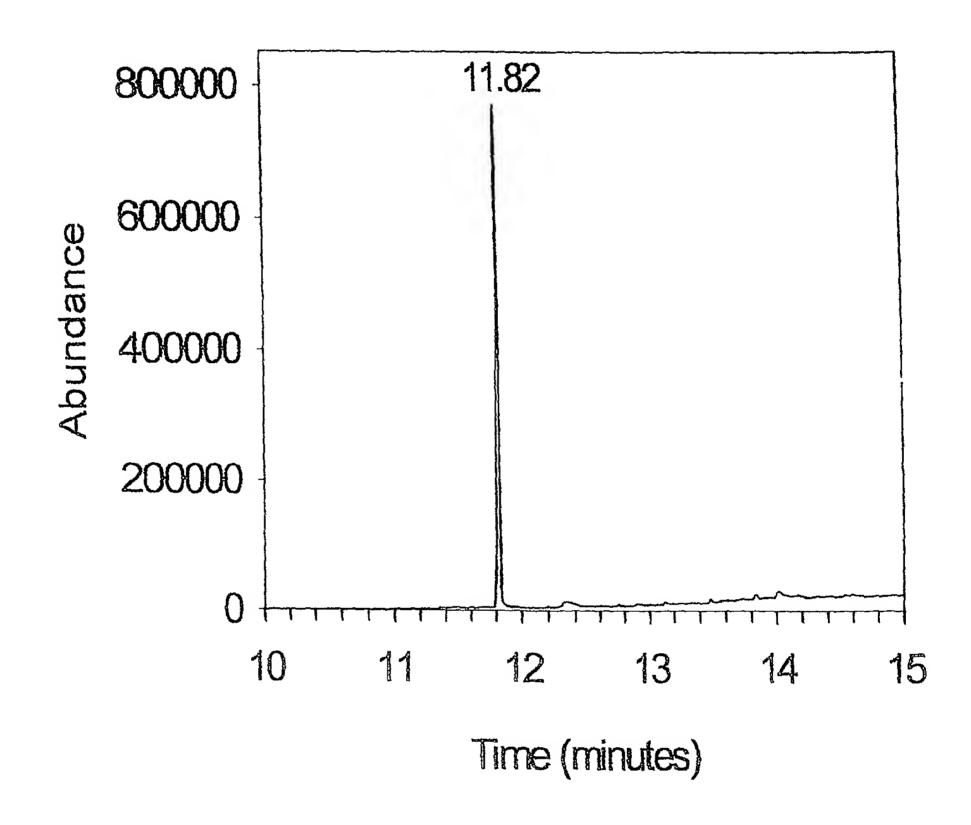


FIG. 5B



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FIG. 5C



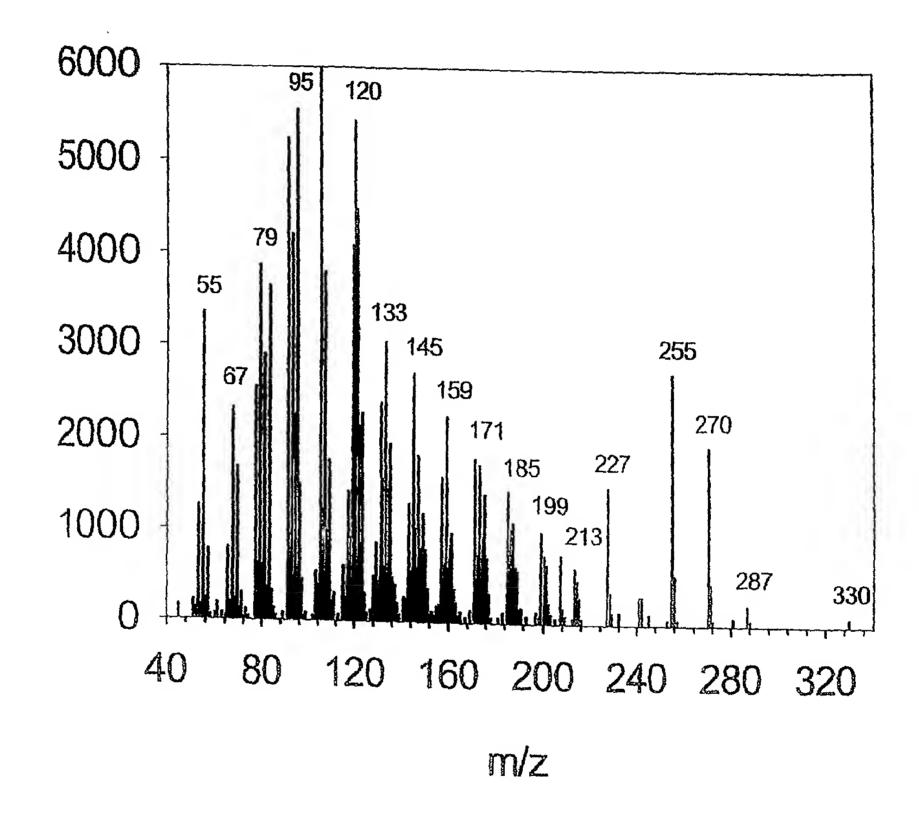


FIG. 5D

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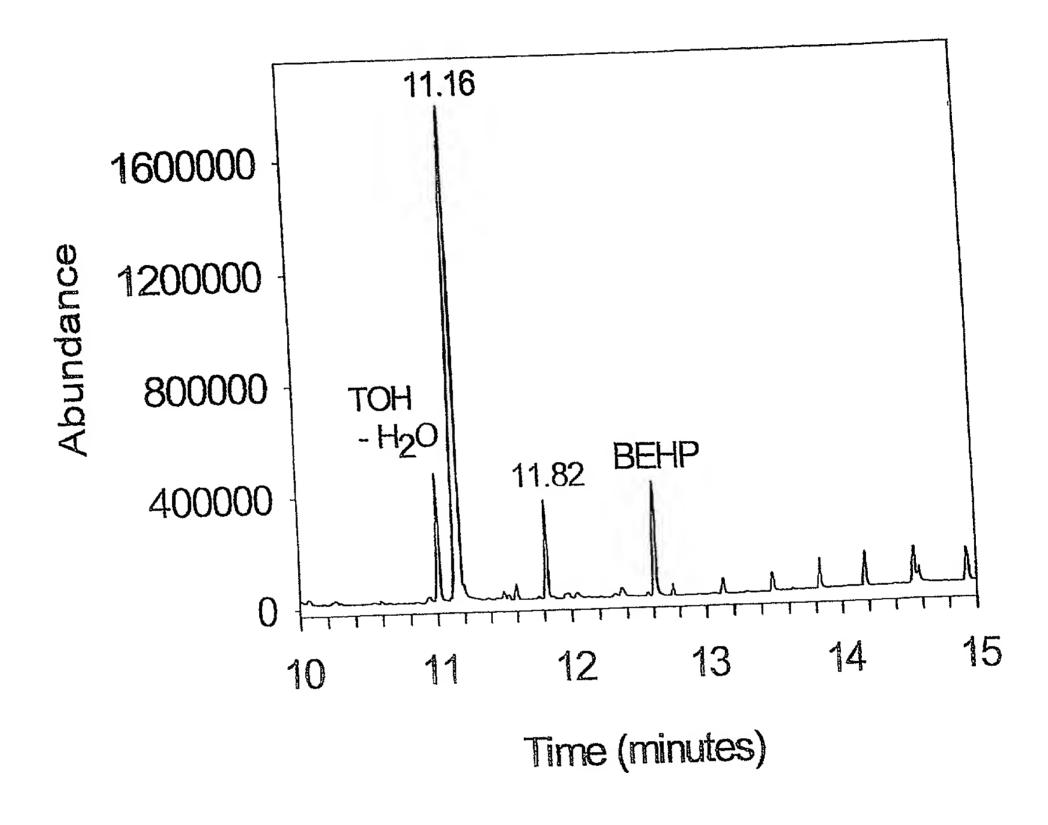


FIG. 5E

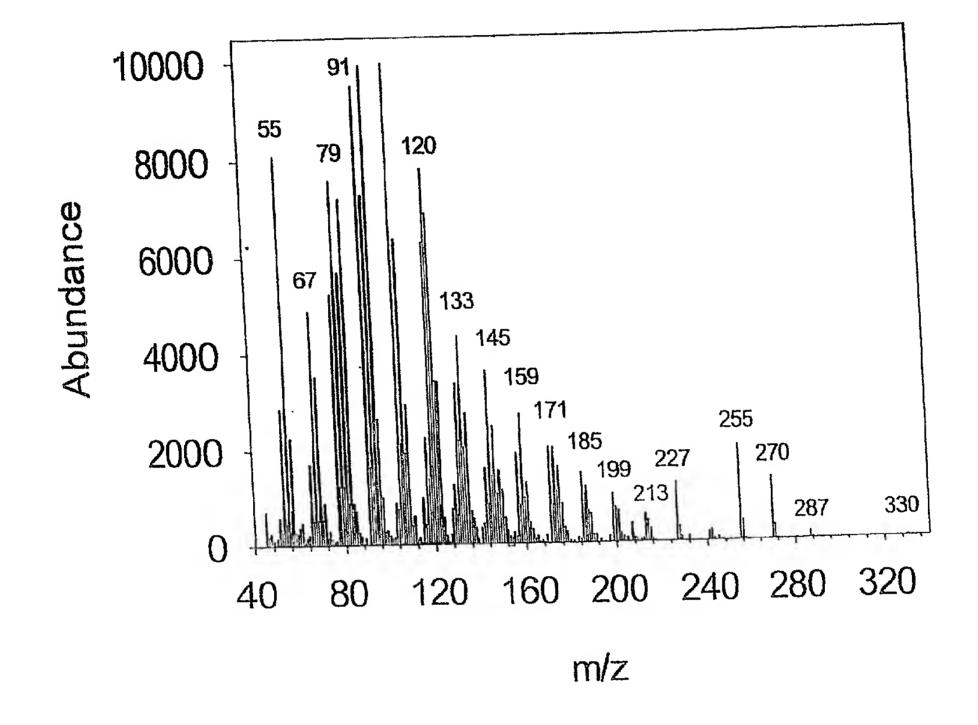


FIG. 5F

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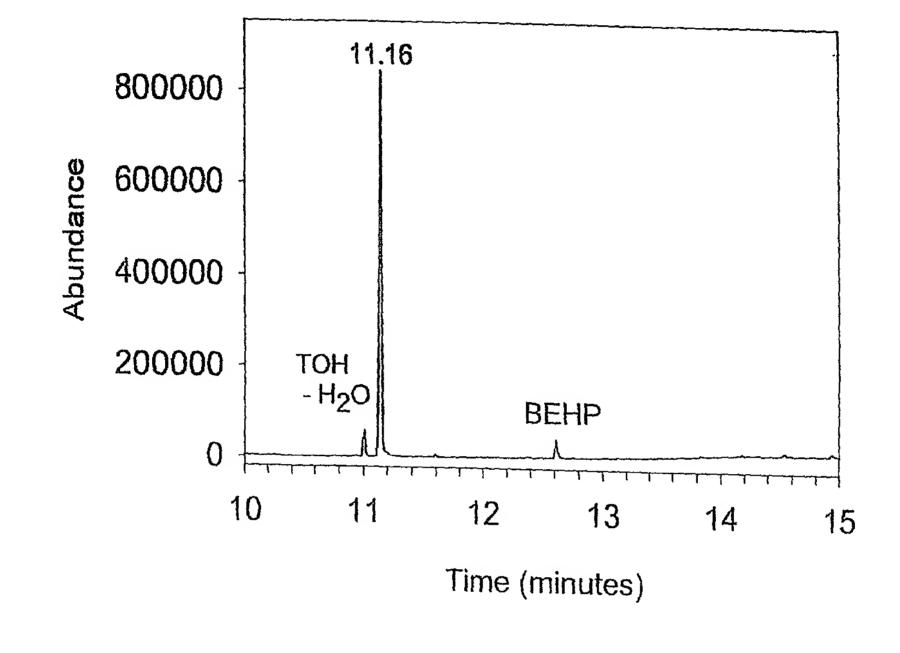


FIG. 5G

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Mailed: September 20, 2001

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TAX1  TAX2  aab61522  aab61523  aab95293  aac17079  aac17079  aac27152  aac27152  aac37152  caac99311  caac964636  caac964636  caac964636  caacb10318  cab10318

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# FIG. 6

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FIG. 6M

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S Ø Σ ₽ Z S S Z Z  $\mathcal{O}$  $\mathbf{Z}$  $\Rightarrow$ Z 区 S S A.  $\mathbf{D}^{t}$ щ  $\Box$  $\alpha$  $\mathbf{z}$ Z Z G  $\Omega_1$ Z >又 Z ß H  $\Sigma$  $\succ$ Z L Ø O! 又 വ  $\Box$ S <u>[--1</u> 1-1 S S ≯ 又 H  $\Rightarrow$ A ы Þ >>Д >又 Z S 又  $\propto$ 二 又 Q T. ≻ × K 回  $\alpha$ S  $\bigcirc$ 又  $\boldsymbol{\vdash}$ Ø  $\vdash$ Σ Σ 딘  $\mathbf{\Sigma}$  $\mathbf{Z}$ H **⊣** 1 Z  $\mathbf{H}$ E⊣ Н  $\Box$ ß Īщ  $\triangleright$  $\circ$ Ø > 1 H Н 工 ₽  $\Box$ Н [±] Ęų Q Z,  $\Box$  $\vdash$ L. O; ጚ Ω 口 [1] [T] F [F] S ഗ O, [T] × 工 ≯ Y 团 Σ  $\mathbf{\Sigma}$  $\mathbf{\Sigma}$ O; G K 工 ĮΤΙ [L] L Н  $\triangleright$  $\Omega^{1}$  $\circ$  $\Omega$  $\Box$ [F] I 3  $\mathbf{z}$ 工 [+] Z Z M H  $\succ$  $\bigcirc$ 又 团 国 Ø Ø 되 [교] · ſzÌ 回 又 S S S > 口 Z S  $\Sigma$ 团  $\alpha$ 又 H 山  $\Box$ 1 ហ Ö Н Q EME H H H H H H <del>[ |</del>  $\triangleright$ Z  $\mathcal{O}$ 工 വ  $\circ$ G O  $\mathcal{O}$ O ល NO: 26) NO: 61) NO: 70) NO: 71) NO: 75) NO: 76) NO: 62) NO: 63) NO: 67) NO: 72) NO: 68) NO: 69 ë S Š Ö ğ ë SEQ D CEQ ES cab10319 (SEQ ID cab40761 (SEQ ID aab61522 (SEQ ID (SEQ ID (SEQ D (SEQ D aac17079 (SEQ ID aac18062 (SEQ ID OEO D (SEQ ID CEQ ID (SEQ ID (SEQ ID cab06427 (SEQ ID (SEQ ID TAX2 aab97723 aac99311 aad12025 cab10318 aab95293 caa64636 caa94432 aab61523 aac27152 caa20531

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Donald L. Stephens, Jr.
Our Ref. No. 4630-59094/DLS/JOC
Inventors: Croteau et al.
For: TRANSACYLASES OF THE PACLITAXEL
BIOSYNTHETIC PATHWAY
Application No. 09/866,570, filed May 25, 2001
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geranylgeranyl diphosphate

taxa-4(20),11(12)-dien- $5\alpha$ -ol

taxa-4(20),11(12)-dien-5α-yl acetate

10-deacetylbaccatin III

baccatin III

Taxol:  $R_1 = Ac$  $R_2 = N-Bz$  phenylisoserinyl

Taxotère R1 = H R2 = N-t-BOC phenylisoserinyl

FIG. 8A

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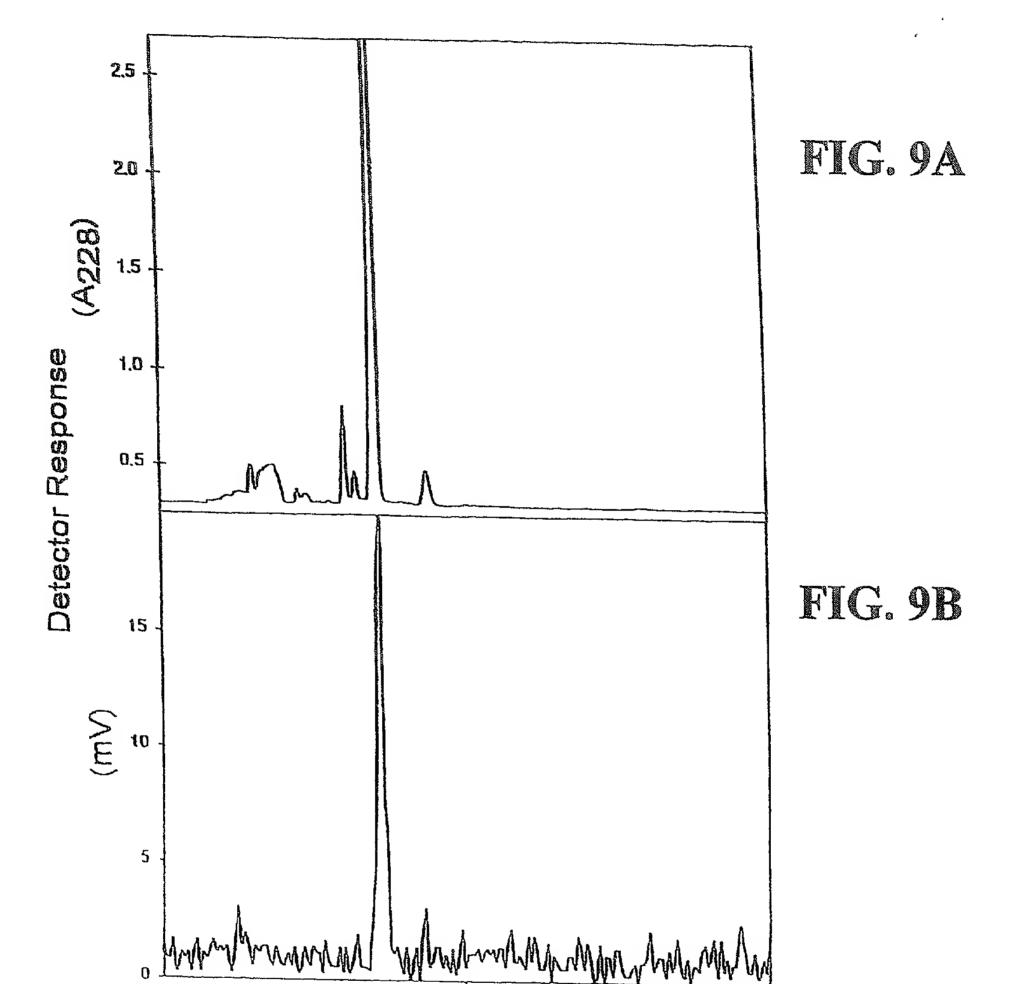
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4(20)-ene-5
$$\alpha$$
-ol 4(20)-ene-5 $\alpha$ -yl acetate 4(20)-epoxy-5 $\alpha$ -yl acetate oxetane

FIG. 8B

E

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Time (minutes)

315

